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1    IMPROVED FORMULATION FOR PROVIDING AN ENTERIC COATING2    MATERIAL

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4    The present invention relates to a formulation for  
5    providing an enteric coating material and in particular  
6    relates to such a material made up of food use approved  
7    materials.

8

9    In many cases it is a requirement of pharmaceutical and  
10   neutraceutical dosage units that they are able to pass  
11   through the stomach intact and only release their  
12   contents further down the GI Tract. This is necessary  
13   when a particular ingredient (or ingredients) of the  
14   dosage unit is unstable in the strongly acidic  
15   environment of the stomach and where the ingredient or  
16   ingredients are intended for release in the slightly  
17   alkaline conditions of the GI Tract beyond the stomach.

18

19   The prior art shows many cases where pharmaceutical  
20   dosage units achieve the abovementioned requirement using  
21   an enteric coating. Enteric coating materials are  
22   material types that are acid resistant, protecting and  
23   preventing the dosage unit from a releasing of the

1 contents into the stomach. However, these coatings  
2 dissolve or disintegrate in the neutral or mildly  
3 alkaline conditions that are encountered beyond the  
4 stomach. In the pharmaceutical industry enteric coatings  
5 are widely used, with a wide choice of enteric materials  
6 such as hydroxypropyl methylcellulose phthalate (HPMCP),  
7 methacrylic acid/methyl methacrylate copolymers (for  
8 example Eudragit™ materials), cellulose acetate phthalate  
9 (cap) and polyvinyl acetate phthalate (PVAP). All of  
10 these enteric materials have been developed over a  
11 considerable period to provide a wide range of organic  
12 solvent soluble materials or aqueous dispersions that  
13 have both excellent coating and enteric properties.  
14 However, manufacturers have had to invest heavily to gain  
15 approval for the use of their materials in the  
16 pharmaceutical industry and rigorous testing of the  
17 materials has been required. Although all of these  
18 products have been through this pharmaceutical approval  
19 route, they have not been considered as viable  
20 propositions for companies to devote similar significant  
21 resources to gain approval for use in the food industry.  
22 Therefore, although these materials are appropriate  
23 enteric materials they are not approved for food use and  
24 cannot legally be used to provide enteric coatings for  
25 non-pharmaceutical dosage units. There are many cases  
26 when it would be useful to provide enteric coatings on  
27 items that are non-pharmaceutical dosage units, for  
28 example for certain health foods etc.

29

30 There are in fact very few materials that are both  
31 approved for food use and can be used as enteric  
32 coatings. An example of a material that is approved for  
33 food use and has been used or suggested as a enteric

1 coating material is Zein. Zein is a prolamine obtained  
2 from corn and is used as a tablet binder or tablet  
3 coating agent. It has in the past been used as an  
4 enteric coating material and is insoluble in water and  
5 most of the common organic solvents including both  
6 acetone and ethanol. It can be dissolved and sprayed as  
7 a film from propylene glycol/water solutions but due to  
8 the high propylene glycol content (typically over 75%)  
9 and high boiling point of propylene glycol, its use  
10 suffers from technical, solution cost and environmental  
11 consideration problems. Zein coats form a very weak film  
12 in acid which, in tests, fail to resist 0.1 N HCl for two  
13 hours. The coating does not dissolve in neutral or  
14 mildly alkaline conditions and therefore does not perform  
15 as a satisfactory enteric coating material. It again has  
16 been suggested that the Zein coat is digested rather than  
17 dissolved in the intestine, which is a rather unusual,  
18 and non-enteric, release mechanism. Therefore Zein is  
19 not particularly useful as an enteric non-pharmaceutical  
20 coating.

21

22 Another possible material that has been suggested is  
23 Shellac. Shellac is an exudate of the lac insect and is  
24 a natural material that is insoluble in water but soluble  
25 in organic solvents including ethanol. The term shellac  
26 covers the range of this type of material. It has been  
27 used as a sealing coat on tablet cores, as a food glaze  
28 and also as a type on enteric coating. As Shellac is  
29 insoluble in acidic conditions but soluble at higher pH  
30 levels it would appear to be suitable as an enteric  
31 coating material. However, reference texts describe  
32 that, in practice, delayed disintegration and delayed  
33 drug release occurs *in vivo* as the Shellac coat is not

1 soluble in the upper intestine. Laboratory trials in  
2 this case have now shown that Shellac does not behave in  
3 a typical enteric coating manner and instead behaves more  
4 like an erodable coating, dissolving as a function of  
5 time rather than of pH.

6

7 Traditionally, Shellac coats have been sprayed from an  
8 organic solution, a disadvantage in terms of solution  
9 cost and environmental protection cost. It is possible  
10 to spray Shellac from an aqueous solution after forming  
11 the Shellac into a water soluble alkali salt, and aqueous  
12 Shellac salt solutions are commercially available. These  
13 commercially available solutions form films that dissolve  
14 in neutral or mildly alkaline conditions and appear, at  
15 first consideration, to overcome the alkaline  
16 insolubility problem of Shellac sprayed from organic  
17 solution. However, unfortunately these films react  
18 rapidly in acid to revert to the free acid Shellac and,  
19 when ingested as a film of a dosage unit, the acidic  
20 conditions in the stomach restore the film to Shellac and  
21 restore the insolubility problem. Shellac films sprayed  
22 as Shellac or as Shellac salts perform similarly and  
23 neither resists acid (0.1 H NCl for two hours) and  
24 rapidly (within one hour) releases the contents of the  
25 dosage unit in neutral or mildly alkaline conditions in  
26 the manner of an enteric coat. Shellac films can be  
27 produced that disintegrate between two and three hours  
28 and would appear to meet the above requirements. However  
29 Shellac films are relatively insensitive to pH and, as  
30 described above, disintegrate between two and three hours  
31 regardless of the solution acidity or alkalinity and  
32 instead behave as erodable films which dissolve as a  
33 function of time.

1

2 It can be seen that it would be beneficial to provide an  
3 enteric coating material that overcomes the problems of  
4 the prior art.

5

6 It is an object of the present invention to provide an  
7 enteric coating material.

8

9 According to a first aspect of the present invention  
10 there is provided an enteric coating formulation  
11 comprising shellac and alginate.

12

13 Preferably the alginate is sodium alginate.

14

15 Preferably the Shellac is in aqueous form.

16

17 Most preferably, the Shellac is in aqueous salt form.

18

19 Preferably the formulation is edible.

20

21 Most preferably the formulation comprises materials that  
22 are approved for food use.

23

24 Optionally, the formulation comprises between 10-90%  
25 Shellac.

26

27 Optionally, the formulation comprises between 10-90%  
28 alginate.

29

30 Preferably, the formulation comprises equal quantities of  
31 Shellac and alginate.

32

1 Preferably, the formulation is in the form of a spray  
2 solution or a suspension.

3

4 Preferably, a low viscosity grade of alginate is used.

5

6 Preferably, the alginate has a viscosity of between 200  
7 and 300 cps.

8

9 Optionally, a plasticiser may be added to the  
10 formulation.

11

12 According to a second aspect of the present invention  
13 there is provided a method of applying an enteric coating  
14 formulation of the type described in the first aspect  
15 wherein the formulation is applied to a dosage unit as a  
16 spray.

17

18 Optionally, the pH of the formulation may be adjusted to  
19 maintain a useable solution / suspension.

20

21 Optionally, the pH of any of the components of the  
22 formulation may be adjusted to maintain a useable  
23 solution / suspension.

24

25 According to a third aspect of the present invention  
26 there is provided a dosage unit comprising enteric outer  
27 coating which is itself comprises Shellac and alginate.

28

29 Preferably the alginate is sodium alginate.

30

31 According to a fourth aspect of the present invention  
32 there is provided a method for preparing an enteric  
33 coating comprising the steps mixing an aqueous solution

1 of an alkali salt of Shellac with an aqueous solution of  
2 sodium alginate.

3

4 In order to provide a better understanding of the present  
5 invention the invention will be described by way of  
6 example only and with reference to the following drawing  
7 in which Figure 1 shows a cross section of a dosage unit  
8 comprising an enteric coating according to the present  
9 invention.

10

11 Sodium alginate is GRAS listed and recognised as a food  
12 additive in Europe. It is used as a stabilising agent,  
13 suspending agent, tablet and capsule disintegrant, tablet  
14 binder and viscosity increasing agent. However, until now  
15 it has never been suggested as a constituent of an  
16 enteric coating material. It is described in the art as  
17 being insoluble below pH3 and slowly soluble in neutral  
18 or alkaline solution and forms aqueous solutions.

19 Therefore it would not appear obvious to use sodium  
20 alginate as part of an enteric coating.

21

22 Neither Shellac, in free acid or alkaline salt form, nor  
23 sodium alginate form films that are acid resistant (where  
24 an acid is 0.1 N HCl) and dissolve or disintegrate in  
25 neutral/mildly alkaline conditions (i.e. pH 6.8 buffer),  
26 i.e. neither performs the function of an enteric coat.

27

28 In the preferred embodiment of the present invention,  
29 Shellac, in the aqueous salt form, and sodium alginate  
30 are be mixed together to provide a formulation which  
31 forms a film that resists acid but disintegrates in  
32 neutral/mildly alkaline conditions. This film has the  
33 properties of an enteric film and is entirely composed of

1 food use acceptable materials. Therefore, it is usable  
2 by the food and neutraceutical industry to coat non-  
3 pharmaceutical (i.e. non-licensed) dosage units where an  
4 enteric coating may still be of great use.

5

6 In alternative embodiments, alginic acid, other salts of  
7 alginic acid (alginates) or alginic acid derivatives such  
8 as potassium alginate could be used in place of sodium  
9 alginate.

10

11 As a preliminary step Shellac may be formed into a  
12 solution of the alkali salt using standard techniques  
13 known in the art. An example of such a technique is to  
14 heat Shellac in water, with stirring, to 50-55°C then,  
15 after dissolution of the Shellac and the addition of 10%  
16 solution of ammonium hydrogen carbonate, the mixture is  
17 heated to 60°C, with stirring for a further 30 minutes.  
18 On cooling, the Shellac remains in solution as the alkali  
19 salt.

20

21 The coating formulation is formed by mixing an aqueous  
22 solution and of an alkali salt of Shellac with an aqueous  
23 solution of sodium alginate. The content of either  
24 material may vary from 10% of one to 90% and will still  
25 demonstrate enteric properties in the film formed. Most  
26 preferably the constituents are present in equal  
27 quantities. The pH of the mixture, or either component  
28 within the mixture, may be adjusted and selected to  
29 maintain a useable solution or suspension.

30

31 The aqueous solution of the alkali Shellac salt may be  
32 formed from Shellac as part of the preliminary process  
33 using methods known in the art.

1  
2 It is also worth noting that sodium alginate is  
3 commercially available as different grades which form  
4 solutions of wildly different viscosities. Preferably,  
5 in this case, a low viscosity grade of sodium alginate  
6 will be used. The preferred viscosity of the sodium  
7 alginate is 200-300cps (centipoise), defined as a  
8 viscosity of a 3% solution in water with a sequestering  
9 agent.

10  
11 A plasticiser may be added to the formulation to modify  
12 the flexibility of the film formed to suit the dosage  
13 requirements. Examples of plasticisers are  
14 triethylcitrate, polyethylene glycol, polypropylene  
15 glycol and glycerin monostearate. The plasticisers would  
16 typically be added in the 5-25% range. The aqueous  
17 Shellac/sodium alginate solution or suspension can, at  
18 suitable concentration which is spraying system  
19 dependent, be sprayed using commercial equipment by  
20 personnel skilled in the art to form films on dosage  
21 units.

22  
23 It can be seen that the present invention has a number of  
24 benefits over the prior art and up until now this  
25 combination of materials has not been known to produce a  
26 film that has enteric properties and is acceptable for  
27 food use. As none of the materials themselves perform in  
28 an enteric manner it is somewhat surprising to find that  
29 the combination of material produces a film that shows  
30 enteric properties, a property possessed by neither of  
31 the components.

1 It should be noted that the embodiments disclosed above  
2 are merely exemplary of the invention which may be  
3 embodied in many different forms. Therefore, details  
4 disclosed herein are not to be interpreted as limiting  
5 but merely as a basis for claims and for teaching one  
6 skills in the art as to the various uses of the present  
7 invention in any appropriate manner.